

g
28. Composition according to claim 26, in which the rutoside is rutin.

29. Composition is solid form and forming a composition according to claim 21 by mixing with water.

REMARKS

Claims 20-29 are pending.

Claims 21-29, newly presented hereby, contain the subject matter of claims 13-19, revised to more clearly define the invention

Claim 21 represents claim 13, with "in particular" deleted, and claim 26 represents claim 16, to effect the correct spelling of "quercitin."

The subject matter of claims 14 and 15 is represented by claims 22-25; claim 14 subject matter is divided as claims 22 and 24, with each of claims 23 and 25 corresponding to claim 15 and depending on claims 22 and 24, respectively.

The objection to claim 16 is overcome by replacement claim 26, which effects the correct spelling of "quercitin."

Reconsideration is requested with respect to the rejection under 35 U.S.C. 112, second paragraph, since the phrase "in particular" does not appear in any of the pending claims.

Claims were rejected under 35 U.S.C. 103(a) based on the combined teachings of U.S. Patent No. 6,316,012 (N'Guyen) and U.S. Patent No. 5,952,373 (Lanzendorfer). Reconsideration is requested.

In the context of a rejection for obviousness under §103, the "*Examiner* bears [both] the initial burden . . . of presenting a *prima facie* case of unpatentability" and "the ultimate burden of persuasion on the issue." *In re Oetiker*, 24 USPQ 1443, 1444 and 1447 (Fed. Cir. 1992), *emphasis, added*. "The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art *would lead* that individual to combine the relevant references. . . . Indeed, the teachings of the references can be combined only if there is some suggestion or incentive to do so." *Ex parte Obukowicz*, 27 USPQ 1063, 1065 (BPA&I 1992)(*emphasis, added*). The "evidence upon which the examiner relies must clearly indicate that a worker of routine skill in this art would view the claimed invention as being obvious." *Ex parte Wolters*, 214 USPQ 735, 736 (BPA&I 1982). The fact that all elements of a claimed invention are known does not, by itself, make the combination obvious. *Ex parte Clapp*, 227 USPQ 972 (BPA&I 1985). As explained by the Board in the decision *Ex parte Levengood*, 28 USPQ2d 1300, 1300-01 (BPA&I 1993)(*emphasis in original*):

In order to establish a *prima facie* case of obviousness, it is necessary for the examiner to present *evidence*,^[1] preferably in the form of some teaching, suggestion, incentive or inference in the applied prior art, that one having ordinary skill in the art *would have been led* to combine the relevant teachings of the applied references in the proposed manner to arrive at the claimed invention [*citations, omitted*].

An argument by the USPTO is "not prior art." *In re Rijckaert*, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). When the

USPTO asserts that there is an explicit or implicit teaching or suggestion in the prior art, it must indicate where such a teaching or suggestion appears *in the reference*. . . . The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient to establish inherency. . . . [S]uch a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection.

28 USPQ2d at 1557, *emphasis added*. "It is facts which must support the legal conclusion of obviousness." *Ex parte Crissy*, 201 USPQ 689, 695 (POBdApp 1976).

The Patent Office has the initial duty of supplying the factual basis for its rejection. It may not, because *it may doubt* that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in the factual basis.

In re Warner, 154 USPQ 173, 178 (CCPA 1967) (*emphasis in original*).

When "the examiner's comments regarding obviousness amount to an assertion that "one of ordinary skill in the relevant art would have been able to arrive at [the claimed] invention because he had the necessary skills to carry out the requisite process steps[,] [t]his is an inappropriate standard for obviousness." *Ex parte Levengood*, 28 USPQ2d 1300, 1301 (BPA&I 1993).

The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification.

In re Fritch, 23 USPQ2d 1780, 1783-84 (Fed. Cir. 1992). "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."

In re Fine, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988).

Differences between the claims and the prior art do not amount to "an obvious design choice," when they "achieve different purposes." *In re Gal*, 25 USPQ2d 1076, 1078 (Fed. Cir. 1992). Where the *optimization* of a claim variable was not recognized in the art as effecting the claimed result, the result is unobvious. *In re Antonie*, 195 USPQ 6, 8 (CCPA 1977). That a difference with the prior art amounts to an alleged "optimal condition . . . is not a substitute for some teaching or suggestion supporting an obviousness rejection." *Rijckaert*, 28 USPQ2d at 1957.

Obviousness is not established by "the rather general urge commonly felt by alert research men to investigate each new . . . process that appears in order to see if it can be used to improve any of the processes in which they are currently interested." *Ex parte Polak*, 83 USPQ 135, 136-137 (POBdApp 1949). "Obvious to experiment" is not the standard for obviousness under §103 of the statute; "selective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings." *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1532 (Fed. Cir. 1988). Moreover, where the practitioner cannot foresee the results, obviousness to try "*with a reasonable chance of success*" does not distinguish over obvious to try as an improper basis for a finding of obviousness under §103. *Ex parte Old*, 229 USPQ 196 (BPA & I 1985) (*emphasis added*).

An "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain conditions were perused.

In re Lilly & Co., 14 USPQ2d 1741, 1743 (Fed. Cir. 1990). A *reasonable expectation of success* is only part of what the PTO must demonstrate to support a rejection for obviousness under §103(a): "Both the *suggestion and* reasonable expectation of success must be founded in the prior art." *In re Vaeck*, 20 USPQ2d 1438, 1441 (Fed. Cir. 1991) (*emphasis added*). A reasonable expectation of success "founded in the prior art" still fails to support a rejection for obviousness, because the requisite "suggestion" is not also found in the prior art. *Id.*

The present claims define a pharmaceutical composition for the prevention and treatment of radiomucositis and chemomucositis induced by radiotherapy or radiochemotherapy. The claimed composition comprises an effective quantity of a flavonoid compound or an isoflavonoid compound in combination with a vehicle, which vehicle is liquid at room temperature, but which vehicle gels at mucous-membrane temperature and adheres to the mucous membrane because of its gelled state.

N'Guyen discloses compositions in the form of solutions or thickened solutions, gels, ointments, emulsions such as creams or milks, powders, and so on. The compositions are to be applied in their initial, preformed state on healthy skin, hair, or mucous membrane, such as buccodental membranes (dentifrices) and ophthalmic membranes (collyria). There is no teaching or suggestion of any kind by N'Guyen relating to a composition that is liquid at room temperature and for use at room temperature, but that gels at mucous-membrane temperature and adheres to the mucous membrane because of its gelled state.

Lanzendorfer discloses a composition for topical administration. This composition can be formulated as a solution, emulsion, stick, aerosol, or gel. As in N'Guyen, there is no kind of

teaching or suggestion in Lanzendorfer for a formulation that is liquid at room temperature, but that gels, to adhere to a mucous membrane, once applied on the mucous membrane, under the effect of the temperature of the mucous membrane..

Therefore, rejected claims 13-20, and replacement claims 21-29, are non obvious under §103(a) with regards to N'Guyen and Lanzendorfer, taken alone or in combination.

Moreover, the cited references do not suggest the use of the ingredients for a composition intended to prevent or treat radiomucositis or chemomucositis induced by radiotherapy or radiochemotherapy.

N'Guyen mentions only ultraviolet radiation. Protection against ultraviolet radiation is, implicitly, the protection sought by the kind of cosmetic composition disclosed by N'Guyen.

While Lanzendorfer teaches its composition is for treating photodermatosis and photodermatitis, there is no teaching or suggestion that the composition would even be of interest in treating, let alone successfully treat, radiomucitis or chemomucositis.

Dermatosis and dermatitis are afflictions of the dermis. As explained, for example, in Stedman's Concise Medical and Allied Health Dictionary, Third Edition (2000), the dermis is a layer of the skin composed of a superficial thin layer that integrates with the epidermy, the stratum papillare, and the stratum reticulare, and it contains blood and lymphatic vessels, nerves and nerve ending glands, and, except for glabrous skin, hair follicles.

On the other hand, the mucosa is a tissue completely different from the dermis. Mucosa is a mucous tissue lining various tubular structures, consisting of epithelium, lamina propria, and, in the digestive tract, a layer of smooth muscles.

Thus, a mucositis is neither a dermatitis nor a dermatosis; the pathologies concern anatomically different and distinct tissues.

Radiodermatitis is a dermatitis caused by overexposure to X-rays or gamma-rays, resulting in ionization of water in the dermis, with dermal changes resembling a thermal injury.

Radiation dermatosis is skin change at the site of ionizing irradiation, particularly, erythema in the acute stage, temporary or permanent epilation, and chronic changes in the epidermis and dermis resembling actinic keratosis.

Thus, the cited references provide no suggestion to use the active principle (flavonoid/isoflavonoid) of the present claims, let alone the precise formulation of the composition according to the present claims, to prevent or treat radiomucositis or chemomucositis in accordance with the invention presently claimed.

Moreover, it should also be borne in mind that the mucosa is often quite difficult to reach, such as, for example, a digestive mucosa, respiratory mucosa, and so on. Mucosa are tissues that cannot be reached as easily as the skin. Damage to the mucosa can lead to afflictions without any apparent lesions of the kind normally occurring on damaged skin or integument. The presently claimed invention unexpectedly provides effective treatment of mucosa damaged by radiation.

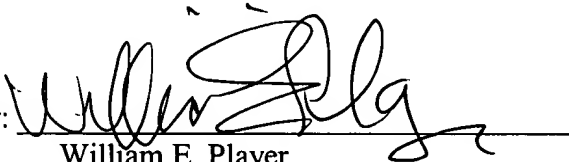
Therefore, the cited references do not suggest to one skilled in the art to use the effective quantity of flavonoid or isoflavonoid to prepare a pharmaceutical composition for the treatment of a radiomucositis or a chemomucositis induced by radiotherapy or radiochemotherapy.

Neither cited reference discloses a pharmaceutical composition comprising an effective quantity of flavonoid/isoflavonoid in a vehicle, which is liquid at room temperature, but which gels at the temperature of the mucous membrane and which adheres to the mucous membrane because its gelled state. Neither cited reference suggests the advantage of such a vehicle in prevention or treatment of mucous membrane pathology.

Favorable action is requested.

Respectfully submitted,

JACOBSON HOLMAN PLLC

By: 
William E. Player
Reg. No.: 31,409

The Jenifer Building
400 Seventh Street, N.W.
Suite 600
Washington, D.C. 20004
(202) 638-6666
Atty Dkt. No.: P66226US0
Date: June 18, 2002
WEP/rdt

R:\HOME\thomas\2002\June\P66226US0-A.mdt